CLAIMS

What Is Claimed Is:

1. A combinatorial library of indolinone compounds, comprising a series of at least ten indolinones that can be formed by reacting oxindoles with aldehydes.

2. The combinatorial library of claim 1 wherein said oxindoles are type A oxindoles.

3. The combinatorial library of claim 1 wherein said aldehydes are type B aldehydes.

4. The combinatorial library of claim 1 wherein said library comprises at least 100 indolinones.

5. The combinatorial library of claim 1 wherein said library comprises at least 1000 indolinones.

6. The combinatorial library of claim 1, wherein most of said indolinones are in the cis conformation.

7. A method of making an indolinone comprising the steps of

(a) creating a combinatorial library of

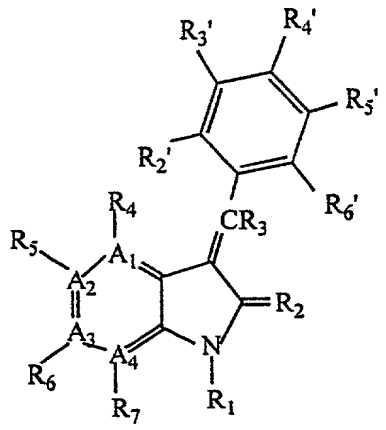
indolinones by reacting a series of oxindoles with a series of aldehydes,

(b) testing said indolinones in biological assays,

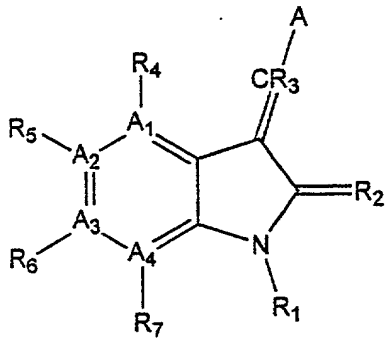
(c) selecting one or more indolinones with favorable activity; and

(d) synthesizing one or more of said indolinones selected in step (c).

8. A compound having formula V or VI



(V)



(VI)

and pharmaceutically acceptable salts, isomers, metabolites, esters, amides, and prodrugs thereof, wherein:

(a) A_1, A_2, A_3, and A_4 are independently carbon or nitrogen;

(b) R_1 is hydrogen or alkyl;

(c) R_2 is oxygen or sulfer;

(d) R_3 is hydrogen;

(e) R_4, R_5, R_6, and R_7 are optionally present and are each independently selected from (i) the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO_2NRR', SO_3R, SR, NO_2, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, $(CH_2)_nCO_2R$, and CONRR' or (ii) any two adjacent R_4, R_5, R_6, and R_7 taken together form a fused ring with the aryl portion of the oxindole-based portion of the indolinone;

(f) R_2', R_3', R_4', R_5', and R_6' are each independently

selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO_2NRR', SO_3R, SR, NO_2, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, $(CH_2)_nCO_2R$, and CONRR';

(g) n is 0, 1, 2, or 3;

(h) R is H, alkyl or aryl; and

(i) R' is H, alkyl or aryl.

(j) A is a five membered heteroaryl ring selected from the group consisting of thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, optionally substituted at one or more positions with alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO_2NRR', SO_3R, SR, NO_2, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, $(CH_2)_nCO_2R$ or CONRR'.

9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound according to Claim 8.

10. A method for treating diseases related to unregulated tyrosine kinase signal transduction, the method

comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to Claim 8.

11. A method for regulating tyrosine kinase signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to Claim 8.